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FEDERAL EXPRESS/STANDARD

November 3, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane - Room 1061
Rockville, Maryland 20852

Re: Comments of Agvar Chemicals Inc. on Docket No. 85N-0214, 64 Fed. Reg. 42873 (August 6, 1999), "180-Day Generic Drug Exclusivity For Abbreviated New Drug Applications"

Gentleperson:

On August 6, 1999, the Food and Drug Administration published a proposed rule to amend the generic drug regulations to establish a triggering period during which an eligible ANDA applicant would have to use or lose 180-day exclusivity, and for other purposes. The notice invited written comments by November 4, 1999.

Agvar Chemicals Inc. is pleased to submit these comments. Agvar Chemicals Inc. is an exclusive distributor of bulk pharmaceutical ingredients made by several major foreign manufacturers of bulk and finished dosage form drugs. Many of Agvar's customers obtain FDA marketing approval for their drug products through abbreviated new drug applications.

Agvar believes that both innovation in drug development and the availability of high quality generic versions of brand name drugs are important to the American public. How the FDA interprets the 180-day exclusivity provision of the Food, Drug, and Cosmetic Act (FDC Act) affects the balance between those goals.

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Agvar believes FDA has made a reasonable attempt to strike an appropriate balance, but that the triggering period approach has disadvantages. Further, FDA has not given consideration to other possible revisions in its Hatch-Waxman regulations that would also address the problems this proposal is meant to address.

1. Triggering period. In general, Agvar supports the proposed triggering period concept. The triggering period eliminates the problem that exists when a previous paragraph IV ANDA indefinitely delays entry of a generic drug product onto the market. A principal objective of the 1984 law was to encourage the development and marketing of generic drugs, consistent with the rights of patent holders. Achieving this objective benefits both the generic drug industry and, more important, the public, through lower drug prices resulting from increased competition.

There are several disadvantages to the triggering period approach. First, it undercuts the value of the 180-day exclusivity period as an incentive to challenging patents. The value of 180-day exclusivity is diminished if the ANDA applicant either cannot take advantage of it, or cannot do so without incurring a significant risk of financial penalties. Because the triggering period may require the ANDA applicant, when a second ANDA is tentatively approved, to "use" the exclusivity even though the first applicant cannot market its drug or can do so only before patent litigation is complete (thereby risking damages if the applicant does not prevail), the value of 180-day exclusivity may be reduced. In that respect, and in some situations, the triggering period

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is inconsistent with the Waxman-Hatch goal of encouraging ANDA applicants to challenge patents.

FDA takes the position that the first ANDA applicant can (by a waiver) sell its right to exclusivity, and thereby realize its value, if it cannot take advantage of it directly. This may not be a practical option in many cases, because it is likely that potential buyers of the exclusivity would also be unable to take advantage of the exclusivity period.

Nevertheless, Agvar supports the triggering period as an improvement over the existing situation. If there is to be a triggering period, Agvar believes that it should be shorter than 180 days. The purpose of the triggering period is not to reward the first paragraph IV applicant, but to expedite generic drug competition. A 60-day triggering period would be more consistent with that objective. Moreover, a longer triggering period is unlikely to ameliorate the disadvantages noted above, and therefore the increased delay provides no off-setting advantage.

2. Orange Book changes. A principal reason why there have been significant difficulties in implementing 180-day exclusivity is FDA's decision to list formulation patents in the Orange Book. This decision may have been legally defensible, but it was not the only one that could have been supported by the statute. If only composition of matter patents (and method of use patents) had been listed, Agvar believes that the majority of difficult 180-day exclusivity issues would not have arisen to begin with. FDA should therefore consider revising its interpretation of which patents qualify for Orange Book

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listing, so that only composition of matter and method of use patents require certification by paragraph IV ANDA applicants.

FDA should also consider adopting a more active approach toward managing the patent listing provisions of the Hatch-Waxman Amendments. There appear to have been a number of questionable patent listings. Because FDA does not review patent listings, there is no deterrent to the listing of inappropriate patents. A weak or spurious patent, or one that does not, in actuality, "claim" the drug in question, acquires a disproportionately high value due to the Hatch-Waxman remedies based on Orange Book listing.

FDA claims it is unable to review proposed patent listings, and therefore has taken the position that it will not do so. Rather than decline to exercise its responsibility, FDA should obtain the necessary resources to carry it out.

Agvar encourages FDA to consider changing its Orange Book patent listing rules as an alternative to creating a triggering period, or as an additional mechanism for carrying out the purpose of the Hatch-Waxman Amendments.

3. Alternative interpretations of the triggering event criteria for 180-day exclusivity. The proposed triggering period approach is intended to solve the problem of delayed generic drug market entry that is caused, in part, by the fact that the triggering events for 180-day exclusivity are within the control of persons – the first paragraph IV applicant and the NDA or patent holder – whose interests may be advanced if the ANDA

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drug is not marketed, or if a patent challenge is not carried through to a decision on the merits.

Agvar believes that this problem can be addressed by interpreting the triggering event provisions to cover situations that are functionally the same as those FDA currently recognizes as meeting the statutory criteria. Specifically:

a. Agreement, settlement, consent decree. If the paragraph IV ANDA applicant enters into an agreement, settlement, or consent decree pursuant to which the generic drug is not to be marketed, FDA could regard the arrangement as the equivalent either of a voluntary withdrawal of paragraph IV certification or as an act of commercial marketing.

b. Estoppel. If the patent that is the subject of the first paragraph IV ANDA's certification becomes unenforceable against any paragraph IV ANDA applicant for that drug, FDA could regard that event as equivalent to a court decision. A patent could become unenforceable, for example, by estoppel against a patent holder that notifies a subsequent paragraph IV applicant that the patent is not infringed. This result is indistinguishable from a favorable court decision in a lawsuit involving a paragraph IV ANDA, including one not involving the first paragraph IV ANDA. Such a court decision is a triggering event under FDA's existing interpretation.

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These interpretations of the 180-day exclusivity triggering events would not solve all of the problems that the triggering period approach would solve. However, they would solve many of them. Moreover, they might be more legally defensible than the triggering period, and would be less likely to undercut the value of generic drug exclusivity.

4. Lawsuit requirement. Agvar disagrees with FDA's proposal to abandon the requirement that a paragraph IV ANDA applicant must be sued to qualify for 180-day exclusivity. As a matter of policy, a generic drug company should not be eligible for exclusivity merely for submitting a paragraph IV certification, when in many cases there is no risk involved and little benefit to the public. Because FDA itself has chosen to list formulation patents in the Orange Book, generic drug companies can often submit certifications of noninfringement of a listed patent without significant risk of disagreement from the patent holder. Although the public benefits from quicker availability of a particular generic drug in that situation, the patent remains as a barrier to entry of other generic products, because the ANDA applicant did not need to challenge it. The 180-day exclusivity incentive was meant to encourage generic drug companies to challenge weak patents for the general benefit of consumers, by removing barriers to entry of generic drugs into the marketplace. Therefore, 180-day exclusivity should not be awarded when such a challenge has not occurred.

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Furthermore, as a legal matter, FDA's interpretation of the 180-day exclusivity provision as not requiring the first paragraph IV ANDA applicant to be sued is incorrect. Agvar explained this conclusion in its October 12, 1998, comments in Docket No. 98 D-0481.

5. Implementation plan. FDA proposes to apply the provisions of the rule to ANDAs pending as of the effective date of the rule and to subsequently submitted ANDAs. Agvar believes that pending ANDAs, and subsequent ANDAs for the same reference listed drug, should not be subject to the new rules. Generic drug applicants have made, and must continue to make, business, regulatory, and litigation decisions based on the regulations and interpretations currently in effect. It would be unfair and disruptive for FDA to change the rules for ANDAs submitted on the basis of those decisions after they have been made.

Cordially yours

AGVAR CHEMICALS INC

Agnes Varis
President

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